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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/552,723 | 10/11/2005 | Veronique Coxam | P70904US0 | 6839 |

136 7590 12/24/2008

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| EXAMINER | |
|---|---|
| FRAZIER, BARBARA S | |
| ART UNIT | PAPER NUMBER |
| 1611 | |
| MAIL DATE | DELIVERY MODE |
| 12/24/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/552,723 | COXAM ET AL. | |
| | Examiner | Art Unit | |
| | BARBARA FRAZIER | 1611 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 October 2008 and 10 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *3,6,15,17,20 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,7-14,16,18,19,21-23,25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/27/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

1. Claims 1-26 are pending in this application. Addition of new claims 25 and 26 is acknowledged.

***Election/Restrictions***

2. Applicant's election with traverse of Group I, claims 1, 2, 4-14, 16, and 18-23, drawn to a method for inhibiting bone resorption with oleuropein, and the species osteoporosis, in the reply filed on 10/8/08 is acknowledged. The traversal is on the ground(s) that the claims of Groups I and II can be examined together without significant burden, and that the examples detailed in the specification show the simultaneous inhibition of bone resorption and stimulation of bone formation by oleuropein. This is not found persuasive because, **under PCT Rule 13.2**, the groups lack the same or corresponding special technical feature.

All of the claims are drawn to oleuropein, which is known, as evidenced by Hamdi et al (US 2003/0004117), which teaches administration of oleuropein in therapeutically effective amounts to treat inflammatory conditions (see Abstract). Therefore, the instant claims do not have a special technical feature and thus the claims lack unity.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 3, 15, 17, and 24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable

generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/8/08.

4. Claims 6 and 20 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/8/08.

5. Claims 1, 2, 4, 5, 7-14, 16, 18, 19, 21-23, 25, and 26 are examined.

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**9. Claims 1, 2, 4, 5, 7-14, 25, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockwood (US Patent 7,445,807), as evidenced by Nachman (US Patent 5,714,150).**

The claimed invention is drawn to a method for inhibiting bone resorption in humans or animals comprising the administration to a subject in need thereof a composition comprising oleuropein (see claim 1). Applicants have elected osteoporosis as the disease to be treated (see claim 7).

Lockwood teaches agglomerated granular protein-rich nutritional supplements, for use by specific groups of individuals (abstract). Lockwood teaches that one group to be treated include postmenopausal women, who are particularly susceptible to osteoporosis (col. 1, lines 35-38), and teaches supplements designed for women (columns 13 and 14). The supplements may comprise edible plant extracts, including olive leaf extract (col. 9, lines 28-37). Olive leaf extract is known to inherently contain oleuropein; as evidence, Nachman teaches a method of producing olive leaf extract known as oleuropein with valuable medicinal properties (see abstract and column 1). Therefore, one skilled in the art of edible plant extracts would envisage oleuropein from the disclosure of "olive leaf extract" in Lockwood.

Lockwood does not specifically teach that the supplement comprising olive leaf extract inhibits bone resorption.

However, it would have been obvious to a person having ordinary skill in the art at the time the invention was made to use the supplement taught by Lockwood to treat bone resorption; thus arriving at the claimed invention. One skilled in the art would be motivated to do so because Lockwood fairly teaches and suggests supplements for women, including women susceptible to osteoporosis, and Lockwood also fairly teaches and suggests the incorporation of edible plant extracts, including olive leaf extract, in said supplements. Thus, one skilled in the art would be motivated to select the use of olive leaf extract in the supplement for women by routine experimentation, in order to optimize the intended use of the resulting supplement, which includes making women less susceptible to osteoporosis, thereby inhibiting bone resorption.

Regarding claim 2, Lockwood teaches that the supplement is in oral unit dosage form (abstract).

Regarding claims 4, 5, and 7, Lockwood teaches that the supplements may be used for postmenopausal women which are particularly susceptible to osteoporosis (col. 1, lines 35-38); said women would naturally seek to prevent bone disorders, including bone loss which occurs with aging and disorders associated with unbalanced bone formation-bone resorption ratio. Said women also might suffer from type I or type II osteoporosis or secondary osteoporosis.

Regarding claims 8 and 9, Lockwood teaches that the supplement may be in the form of a rapidly dissolvable wafer or dissolved in a liquid (column 19); said forms reasonably read on "a food composition or beverage" in wet or dry form.

Regarding claims 10-13, Lockwood teaches that the extract may be from olive leaf (i.e., *olea europaea*).

Regarding claim 14, Lockwood teaches that the supplements for women may comprise 50 mg of edible plant extracts (col. 14, line 32). While Lockwood does not explicitly state that the supplements are administered daily, Lockwood does teach that certain components are formulated according to the Recommended Daily Allowance (for example, see col. 9, lines 5-10), and therefore one skilled in the art would reasonably expect that the supplements are administered daily.

Regarding claims 25 and 26, Lockwood teaches that the supplement may be in the form of a rapidly dissolvable wafer, including a combination of carbohydrate and non-caloric sugar substitute (col. 19, lines 21-26). Said form reasonably reads on "confectionary product" and "cookie".

**10. Claims 1, 16, 18, 19, and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamdi et al (US 2003/0004117) in view of Katori et al (Inflamm. Res. 49 (2000), pp. 367-392).**

The claimed invention is delineated above (see paragraph 6).

Hamdi et al teach methods for inhibiting angiogenesis comprising administering oleuropein and/or the products of its hydrolysis in therapeutically effective amounts; said methods may be utilized to treat a wide variety of inflammatory conditions (abstract).

Hamdi et al do not specifically teach administering oleuropein or a derivative thereof to inhibit bone resorption.

Katori et al teach that COX-2 has been reported in several pathophysiological states, including angiogenesis and bone absorption (abstract).

It would have been obvious to a person having ordinary skill in the art at the time the invention was made to use oleuropein to inhibit bone resorption; thus arriving at the claimed invention. One skilled in the art would be motivated to do so because the skilled artisan would reasonably expect that compounds known to inhibit one pathophysiological state in which COX-2 is present (i.e., angiogenesis, as taught by Hamdi et al) would also inhibit another pathophysiological state in which COX-2 is present (i.e., bone resorption, as taught by Katori et al). Furthermore, the populations of subjects with angiogenesis and bone resorption are not mutually exclusive, i.e., one would reasonably expect at least a portion of those with angiogenesis would also suffer bone loss. Therefore, one skilled in the art would reasonably expect that, when oleuropein is administered to inhibit angiogenesis, bone resorption is also inhibited.

Regarding claim 16, Hamdi et al teach that a pharmaceutical composition of oleuropein may be administered (paragraph 15).

Regarding claims 18, 19, and 21, Hamdi et al teach that a disease that can be treated by administration of oleuropein is rheumatoid arthritis (paragraph 67). One

skilled in the art would reasonably expect that said subjects would also seek to prevent bone loss that occurs with aging and/or a pathology associated with an unbalanced bone formation-bone resorption ratio and/or might suffer from osteoporosis.

Regarding claim 22, Hamdi et al teach that the compositions may be in a suitable form for oral, parenteral, intraperitoneal, or intradermal administration (paragraph 74).

Regarding claim 23, Hamdi et al teach that the compositions may be administered orally (paragraph 74) in an amount of approximately 0.030 g to 20 g (i.e., 30-20,000 mg). This amount overlaps that of the claimed invention, and one skilled in the art would be motivated to manipulate the amount of oleuropein from within said ranges by routine experimentation, in order to optimize the therapeutic effect of the resultant composition.

***Conclusion***

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BARBARA FRAZIER whose telephone number is (571)270-3496. The examiner can normally be reached on Monday-Thursday 9am-4pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571)272-0614. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BSF

/Sharmila Gollamudi Landau/
Supervisory Patent Examiner, Art Unit 1611